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JACOBSON, HOLMAN

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NO. 446 P. 1

GROUP 1600

Attorney Docket No. P61813US0

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of Peet KASK

Via facsimile

703-872-9306

Art Unit 1639

Application No. 09/029,830

Filed: March 10, 1998

Examiner BAKER, Maurie Garcia

For METHOD OF ANALYSIS OF SAMPLES BY DETERMINATION OF A FUNCTION OF SPECIFIC BRIGHTNESS

TRANSMITTAL

Commissioner for Patents
Washington, D.C. 20231

Sir:

Transmitted herewith by facsimile please find Response.

Small Entity status of this application under 37 CFR 1.9 and 1.27 has been established.

Fee Calculation						
	N ^o of Claims		Excess Claims	Paid Excess Claims Of Record	Small Entity Fee	Large Entity Fee
Total		⊖ 20 =			⊗ \$9 = \$	⊗ \$18 = \$
Ind.		⊖ 3 =			⊗ \$42 = \$	⊗ \$84 = \$
() Multiple Dependent Fee (First Presentation)					⊗ \$140 = \$	⊗ \$280 = \$
Excess Claims Fee					\$	\$
Extension of Time Fee					\$	\$
Other:					\$	\$
Total Fee Due					\$	\$

A check for \$ is attached.

Charge \$ to Deposit Account No. 06-1358.

X If a petition for extension of time is necessary but not enclosed, the Commissioner is petitioned to extend the time for response. The Commissioner is authorized to charge payment of any fees associated with this communication to Deposit Account No. 06-1358.

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Date: December 26, 2002

By:

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WEP:jd

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For METHOD OF ANALYSIS OF SAMPLES BY DETERMINATION OF A FUNCTION OF
SPECIFIC BRIGHTNESS

RESPONSE

Commissioner for Patents
United States Patent and Trademark Office
Washington, D.C. 20231

Sir:

The instant paper transmitted by facsimile responds to the Office Action mailed November 26, 2002.

Claims 29-76 are pending.

Pursuant to the requirement for election of species contained in the Office Action, applicant elects one species from each of Groups 1-7 as follows.

Group 1: Specific sample analyzed (claims 40-49)

Applicant elects as specific sample (i) fluorescent particles (molecules) and (ii) particles (vesicles) carrying binding sites for the fluorescent particles (claims 40, 44, and 49). As a result of the binding interaction between these two particle species, one will detect (a) singular vesicle particles as being very bright, because each vesicle particle binds multiple fluorescent particles, and (b) singular fluorescent particles being significantly less bright than the vesicle particles. Therefore,

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the particles can be grouped into particle species distinguished by their specific brightness (claim 41).

Group 2: Specific detection means

Applicant elects as specific detection means a confocal microscopic set-up in accordance with claim 35.

Group 3: Specific distribution function of the number of photon counts

Applicant elects as specific distribution function of the number of photon counts the species per time interval in which the time intervals are of defined length (see claim 29). The distribution function of the number of photon counts means the relative number of events when a particular number of photon counts is observed (page 7 of the specification).

Group 4: Specific distribution function of specific brightness

Applicant elects as specific distribution function of specific brightness of particles, the particles being (i) vesicles with fluorescent molecules bound to binding sites of the vesicles and (ii) single fluorescent particles (claims 29, 40, 41, 44, and 49). A mixture of two fluorescent species can be characterized by four parameters: the concentrations and specific brightness of the two species of particles, see claim 63 (page 4 of the specification).

Group 5: Specific modeling method

Applicant elects as specific modeling method least squares fitting as the basic method for determining distributions of number of photon counts, wherein in the fitting process a priori information on the sample is used (claim 64 and page 12 of the specification). Prior to the analysis,

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according to claim 62, parameters of the equipment are determined from an experiment on single species. Fit parameters of this experiment are parameters of the spatial brightness function, as well as a concentration and a specific brightness of the single species, see claim 63. As parameters of the spatial brightness function, one may select convergence angle of the laser beam and pinhole diameter, according to claim 33. These parameters (together with the fixed wavelength of the laser light) are suited for calculating sizes of volumes corresponding to a selected set of spatial brightness values (claim 31). The determined parameters of the spatial brightness function, characterizing the equipment, are means of analysis of samples of unknown composition, in particular mixtures of (i) fluorescent molecules capable of binding to vesicles; and (ii) vesicles each having bound a number of fluorescent molecules. When fitting the measured distribution of the number of photon counts from a particular sample, the fit parameters are two concentrations and two specific brightness values, while background count rate as well as the spatial brightness parameters are fixed at pre-determined values.

Group 6: Specific spatial brightness function

Applicant elects as spatial brightness function the modeling parameters of convergence angle of the laser beam and pinhole diameter (claim 33). These parameters (together with the fixed wavelength of the laser light) are suited for calculating sizes of volumes corresponding to a selected set of spatial brightness values (claim 31).

Group 7: Arrangement of measurement volumes (claims 56-59)

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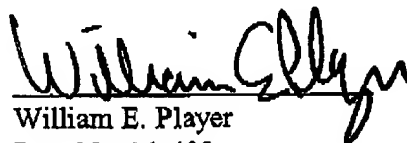
Applicant elects as arrangement measurement volumes (from claims 56-59) a laser beam split into four beams, the four spots are studied in parallel, using four microscope objectives, in order to increase the efficiency of data collection. The four samples are selected on a sheet with 2-dimensional arrangement of wells (claims 56 and 57).

Favorable action is requested.

Respectfully submitted,

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